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Application No.: 09/536,841 Group Art Unit: 1634

Filed: March 27, 2000 Examiner: Ethan C. Whisenant

Confirmation No.: 4992

Title: UNIVERSAL ARRAYS

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AMENDMENT AFTER FINAL REJECTION UNDER 37 C.F.R. 1.116

Box AF
Assistant Commissioner for Patents
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Sir:

This Amendment After Final Rejection is being filed in response to the Final Office Action mailed from the U.S. Patent and Trademark Office on February 27, 2002, in the above-identified application.

As a preliminary matter, Applicants note in Item 1 of the Office Action that the Examiner states that Applicants' response to the Office Action mailed from the United States Patent and Trademark Office on March 22, 2001, "was received on 7 Jan 1997 and has been entered as

paper no. 3." This is believed to be a clerical error because Applicants mailed their response by Certificate of Mailing procedure on September 24, 2001, and the postcard receipt was date-stamped September 28, 2001, by the United States Patent and Trademark Office.

An extension of time for filing a Notice of Appeal from the Final Office Action dated February 27, 2002, is respectfully requested. A Notice of Appeal and a Petition for Extension of Time and the appropriate fee are being filed concurrently with this amendment. Also filed concurrently is a Third Supplemental Information Disclosure Statement.

Please amend the application as follows:

In the Claims

Please amend the claims as follows:

2. (Twice Amended) A kit comprising:
- (a) an array comprising one or more oligonucleotide tags fixed to a solid substrate, wherein each oligonucleotide tag comprises a unique known arbitrary nucleotide sequence of sufficient length to hybridize to a locus-specific tagged oligonucleotide;
 - 3 (b) one or more locus-specific tagged oligonucleotides, wherein each locus-specific tagged oligonucleotide has at its first (5') end nucleotide sequence which hybridizes to the arbitrary sequence of a corresponding oligonucleotide tag on the array, and has at its second (3') end nucleotide sequence complementary to target polynucleotide sequence in a sample wherein the last nucleotide at the 3' end of the locus-specific tagged oligonucleotide hybridizes exactly one nucleotide before the nucleotide to be queried in the target polynucleotide sequence; and
 - (c) at least two labeled dideoxynucleotides, each of which is distinctly labeled.
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20. (Twice Amended) A kit comprising:
- 20 (a) a pair of primers which when in the presence of a DNA polymerase amplify a region of double stranded DNA, wherein the region comprises a polymorphic locus; and

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- (b) an extension primer which comprises a 3' portion which is complementary to a portion of the region of double stranded DNA and a 5' oligonucleotide portion which is not complementary to the region of double stranded DNA, but which is complementary to a unique known sequence of an oligonucleotide tag fixed to a solid substrate, wherein the extension primer is complementary to the 3' nucleotide sequence of the polymorphic locus, and wherein the last nucleotide at the 3' end of the extension primer hybridizes exactly one nucleotide before the polymorphic locus; and
 - (c) at least two labeled dideoxynucleotides, each of which is distinctly labeled.

21. (Twice Amended) A kit comprising in a single container two or more sets of primers, each set comprising:

- (a) a pair of primers which when in the presence of a DNA polymerase amplify a region of double stranded DNA, wherein the region comprises a polymorphic locus; and
- (b) an extension primer which comprises a 3' portion which is complementary to a portion of the region of double stranded DNA and a 5' oligonucleotide portion which is not complementary to the region of double stranded DNA, but which is complementary to a unique known sequence of an oligonucleotide tag fixed to a solid substrate, wherein the extension primer is complementary to the 3' nucleotide sequence of the polymorphic locus, and wherein the last nucleotide at the 3' end of the extension primer hybridizes exactly one nucleotide before the polymorphic locus;

and at least two labeled dideoxynucleotides, each of which is distinctly labeled.

22. (Twice Amended) A kit comprising in a single container:

- (a) a set of primers, comprising:
 - (1) a pair of primers which when in the presence of a DNA polymerase amplify a region of double stranded DNA, wherein the region comprises a polymorphic locus; and
 - (2) an extension primer which comprises a 3' portion which is complementary to a portion of the region of double stranded DNA and a 5' oligonucleotide

portion which is not complementary to the region of double stranded DNA, but which is complementary to a unique known sequence of an oligonucleotide tag fixed to a solid substrate, wherein the extension primer is complementary to the 3' nucleotide sequence of the polymorphic locus, and wherein the last nucleotide at the 3' end of the extension primer hybridizes exactly one nucleotide before the polymorphic locus;

- (b) at least two labeled dideoxynucleotides, each of which is distinctly labeled; and
- (c) a solid support comprising a probe which is attached to a solid support, wherein the probe is complementary to the 5' portion of the extension primer.
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Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - ii).

REMARKS

Claim Amendments

Claim 2 has been amended to recite that the kit includes at least two labeled dideoxynucleotides. Support for this amendment can be found in the Specification, for example, at page 3, lines 11-12.

Claim 20 has been amended to recite a kit comprising the primers and further comprising at least two labeled dideoxynucleotides, each of which is distinctly labeled.

Claims 21 and 22 have been amended to be independent and to incorporate the claim language of Claim 20. No new matter has been added.

Reconsideration of Finality

Applicants thank the Examiner for conferring by telephone on June 20, 2002, regarding reconsideration of the finality of the last Office Action in view of the new rejection of Claim 21 under 37 C.F.R. § 112, second paragraph for indefiniteness. In the telephone conversation, the Examiner indicated his willingness to reconsider the finality of the last Office Action.

Specifically, Applicants believe that the rejection of Claim 21 under 35 U.S.C. § 112, second paragraph, is not a rejection necessitated by Applicants' amendment. The language which is the subject of the rejection ("two or more of the sets of primers of Claim 20") was present in Claim 21 prior to Applicants' amendment. Notwithstanding Applicants' belief

(detailed below) that this rejection should be reconsidered and withdrawn, Applicants nonetheless believe that the Office Action mailed on February 27, 2002 is not properly made final in view of this rejection. Reconsideration is respectfully requested.

Third Supplemental Information Disclosure Statement

Applicants also request consideration of the reference cited in the Third Supplemental Information Disclosure Statement submitted concurrently with this Amendment. In view of Applicants' belief that the Office Action mailed on February 27, 2002 is not properly made final, Applicants request that the SIDS be considered under 37 C.F.R. § 1.97(c). The appropriate fee under 37 C.F.R. § 1.17(p) is submitted herewith.

Rejection of Claims 21-25 Under 35 U.S.C. §112, Second Paragraph

Claims 21-25 are rejected by the Examiner under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as their invention.

Specifically, the Examiner has rejected Claim 21 as being indefinite in the phrase "two or more of the sets of primers of Claims 20." The Examiner states that Claim 20 is directed to a kit which does not explicitly recite any primers. Applicants respectfully point out that Claim 20 was in fact directed to a "set of primers for use in determining a ratio of nucleotides present at a polymorphic locus" and not to a kit.

Nonetheless, Applicants have amended Claim 21 to recite a primer set comprising (a) a pair of primers which, when in the presence of a DNA polymerase, amplify a region of double-stranded DNA, wherein the region comprises a polymorphic locus, and (b) an extension primer which comprises a 3' portion which is complementary to a portion of the region of double stranded DNA and a 5' oligonucleotide portion which is not complementary to the region of double stranded DNA, but which is complementary to a unique known sequence of an oligonucleotide tag fixed to a solid substrate, wherein the extension primer is complementary to the 3' nucleotide sequence of the polymorphic locus, and wherein the last nucleotide at the 3' end of the extension primer hybridizes exactly one nucleotide before the polymorphic locus. Applicants believe Claim 21, as amended, even more particularly points out and distinctly claims the subject matter which Applicants regard as the invention.

The Examiner has also rejected Claim 22 as being indefinite, stating that the phrase “and dideoxynucleotide” lacks proper antecedent basis in Claim 20. Applicants have amended Claim 22 to independent form, obviating this rejection.

In view of the amendments, Applicants believe Claim 21 and Claim 22 and dependent Claims 23-25 even more particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 2 and 20 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 2 and 20 under 35 U.S.C. § 103(a) as being unpatentable over Ugozzoli *et al.* (GATA 9(4): 107-112 (1992); Ref. # U) in view of the Stratagene Catalog (p. 39 (1998); Ref. # W).

According to MPEP § 706.02(j), there are three basic criteria which must be met in order to establish a *prima facie* case of obviousness:

First, there must be some suggestion or motivation in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations.

Ugozzoli *et al.* teach a method of detection for the two-allele polymorphism of the human tyrosinase gene (Abstract). Claim 2, as amended, is drawn to a kit comprising an array of one or more oligonucleotide tags fixed to a solid substrate and one or more locus-specific tagged oligonucleotides, wherein each locus-specific tagged oligonucleotides has at its 5' end a sequence which hybridizes to the arbitrary sequence of a corresponding oligonucleotide tag on the array, and at its 3' end a nucleotide sequence complementary to the target polynucleotide sequence in a sample, wherein the last nucleotide at the 3' end of the locus-specific tagged oligonucleotide hybridizes exactly one nucleotide before the target nucleotide to be queried, and at least two labeled dideoxynucleotides (ddNTPs). The teachings of Ugozzoli *et al.* are specific to the two-allele polymorphism of the human tyrosine gene. Ugozzoli *et al.* do not teach the use of labeled dideoxynucleotides, see, for example, page 109 under section heading AS-PE, wherein Ugozzoli *et al.* use labeled dGTP and TTP, not ddNTPs.

The Stratagene Catalog merely lists kits for general gene characterization. It does not teach or suggest the primers as recited in the instant claims in combination with a labeled dideoxynucleotide. Applicants do not concede that the cited references are properly combined. However, even in combination, Ugozzoli *et al.* and the Stratagene Catalog fail to teach or suggest all the claim limitations of the present invention, because even if the components taught by Ugozzoli, *et al.* were formulated into a kit, they would still fail to teach or suggest a kit comprising the primers of the present invention in addition to at least two ddNTPs. Therefore, a *prima facie* case of obviousness has not been established.

Claim 20 is drawn to kit comprising (a) a pair of primers which when in the presence of a DNA polymerase amplify a region of double stranded DNA, wherein the region comprises a polymorphic locus, and (b) an extension primer which comprises a 3' portion which is complementary to a portion of the region of double stranded DNA and a 5' oligonucleotide portion which is not complementary to the region of double stranded DNA, but which is complementary to a unique known sequence of an oligonucleotide tag fixed to a solid substrate, wherein the extension primer is complementary to the 3' nucleotide sequence of the polymorphic locus, and wherein the last nucleotide at the 3' end of the extension primer hybridizes exactly one nucleotide before the polymorphic locus and (c) at least two dideoxynucleotides, each of which are distinctly labeled.

Ugozzoli *et al.* do not teach or suggest Claim 20, as amended. Ugozzoli *et al.* do not teach a method using dideoxynucleotides, nor do Ugozzoli *et al.* teach a kit comprising the primers of the present invention and at least two labeled dideoxynucleotides. Furthermore, the Stratagene Catalog only lists kits for the general characterization of genes. Again, there is no teaching or motivation to combine the references of Ugozzoli *et al.* and the Stratagene Catalog, and moreover, the combination of Ugozzoli *et al.* and the Stratagene Catalog fails to teach all of the claim limitations of the invention. Even if the primers of Ugozzoli *et al.* were formulated into a kit, they would still fail to teach a kit comprising the primers of the present invention in addition to at least two labeled ddNTPs. Thus, a *prima facie* case of obviousness has not been established. Reconsideration and withdrawal of the rejection are respectfully requested.

Comment on Claims 21-25

The Examiner states that the patentability of Claims 21-25 has not been addressed due to the claim language of Claims 21 and 22. Applicants have now amended Claims 21 and 22. The

Examiner has also noted that Shumaker (*Human Mutation* 7:346-354 (1996); Ref. # V) teach distinctly labeled ddNTPs. Applicants point out that Shumaker *et al.* do not teach or suggest the use of ddNTPs with the set or sets of primers as disclosed in the present application.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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